Amendments to the Specification:

Please amend the section beginning at page 1, line 3, as follows:

CROSS-REFERENCES TO RELATED APPLICATIONS

This application is a continuation of co-pending United States Patent Application No. 10/056,794, filed January 24, 2002; which application is a continuation of United States Patent Application No. 08/871,488, filed June 9, 1997, which issued as United States Patent No. 6,358,710; ~~This~~which application is a continuation-in-part of United States Patent Application No. 08/660,362, filed June 7, 1996 and abandoned; all of which applications are incorporated by reference herewith in their entirety.

Please replace the paragraph beginning at line 26 of page 6 with the following redlined paragraph:

Figure 2 contains the nucleotide and amino acid sequences of NR-LU-13 light chain (SEQ ID NOS: 16-17) NR-LU-13 and heavy chain (SEQ ID NOS: 14-15) variable regions.

Please replace the paragraph beginning at line 1 of page 7 with the following redlined paragraph:

Figure 3 contains the amino acid sequence of the preferred humanized variable light sequence derived from NR-LU-13 (SEQ ID NO: 17), referred to as humanized NRX451-light.

Please replace the paragraph beginning at line 3 of page 7 with the following redlined paragraph:

Figure 4 contains the amino acid sequence of the preferred humanized variable heavy sequence derived from NR-LU-13 (SEQ ID NO: 15), referred to as humanized NRX451-heavy.

Please replace the paragraph beginning at line 7 of page 7 with the following redlined paragraph:

Figure 5 is an alignment of the heavy (SEQ ID NO: 15) and light (SEQ ID NO: 17) variable regions of NR-LU-13 and the humanized heavy and light variable regions derived therefrom, referred to as NRX451 heavy (SEQ ID NO: 19) and NRX451 light (SEQ ID NO: 18).

Please replace the paragraph beginning at line 6 of page 48 with the following redlined paragraph:

Essentially, the cDNA sequence encoding the variable regions of NR-LU-13 antibody (hybridoma producing the antibody was deposited with American Type Culture Collection (10801 University Blvd., Manassas, VA 20110) as ATCC Accession No. SD3273, converted to ATCC Accession No. CRL-12360 were cloned and sequenced by known methods. The cDNA sequences of the cloned light and heavy sequence of NR-LU-13 are contained in Figure 2. Using these sequences, the amino acid sequence of the Fv region of NR-LU-13 which includes the entire variable light and variable heavy regions was elucidated.

Please replace the paragraph beginning at line 24 of page 52 with the following redlined paragraph:

A second CMV promoter and enhancer region were added using PCR to copy the existing CMV elements followed by insertion into pCDNA3. Specifically, oligonucleotides NX62 (CCTGACGAATTCGTTGACATTGATTATTGAC) (SEQ ID NO: 1) and NX63 (CCTGACGCGGCCGCTTCGATAAGCCAGTAAGC) (SEQ ID NO: 2) were synthesized to anneal to the 5′ and 3′ ends of CMV, respectively. NX62 and NX63 were synthesized to introduce EcoRI and NotI restriction sites, respectively. PCR was performed by standard procedures and the resulting fragment was restriction digested with EcoRI and NotI. Plasmid pCDNA3 was likewise digested and the fragment was inserted by standard procedures well known in the art. The resulting plasmid was designated pCMV4.

Please replace the paragraph beginning at line 6 of page 53 with the following redlined paragraph:

The kappa constant region and preceding intron were isolated from human peripheral blood lymphocyte DNA by PCR. Oligonucleotides NX64 (GTTCGGCTCGAGCACAGCTAGCATTATCTGGGATAAGCATGCTG) (SEQ ID NO: 3) and NX65 (GTTACGGGGCCCCTAACACTCTCCCCTGTTGAAG) (SEQ ID NO: 4) were synthesized to anneal to the intron preceding the constant region exon and the 3′ end of the constant region, respectively. NX64 contained both XhoI and NheI restriction sites. NX65 contained an ApaI restriction site following the constant region stop codon. PCR was performed by standard procedure. The fragment was digested with XhoI and ApaI and inserted into pCMV4 by standard procedures. The resulting plasmid was designated pC4-CK3.

Please replace the paragraph beginning at line 15 of page 53 with the following redlined paragraph:

The human gamma1 constant region, including the preceding intron and succeeding polyadenylation site, was isolated from human plasmacytoma (MC/CAR, ATCC CRL 8083) DNA by PCR. Oligonucleotides NX66 (GTACGCGGATCCCAGACACTGGACG CTG) (SEQ ID NO: 5) and NX67 (CATTCGGAATTCGAACCATCACAGTCTCGC) (SEQ ID NO: 6) were synthesized to anneal to the preceding intron and polyadenylation site, respectively. NX66 contained a BamHI site. NX67 contained an EcoRI site following the polyadenylation site. PCR was performed by standard procedure. The fragment was inserted into pCDNA3 by standard procedures. The resulting plasmid was designated pGamma1-4.

Please replace the paragraph beginning at line 18 of page 54 with the following redlined paragraph:

RNA was extracted from pWE1A2 transfected CHO (dhfr) cells with a commercially available RNA extraction kit (Glass Max, Gibco BRL). Reverse transcriptase-PCR (RT-PCR) was performed as per manufacturer's instructions (Perkin Elmer Cetus). In this

procedure, NX109 (GCTGACGAATTCTCATTTACCCGGAGACAGGGAG) (SEQ ID NO: 7), which anneals to the 3′ terminus of the gamma chain constant region was used to specifically prime a reverse transcriptase reaction in which gamma chain messenger RNA was copied into cDNA. NX109 and NX110 (CCGTCTATTACTGTTCTAGAGAGGTC) (SEQ ID NO: 8), which anneals within the heavy chain variable region, were used to amplify the cDNA generated in the reverse transcription reaction. The PCR primers contained BamHI (NX109) and XbaI (NX110) restriction sites to facilitate cloning. The restricted PCR product was inserted into the plasmid to form p1A2.C1.

Please replace the paragraph beginning at line 6 of page 55 with the following redlined paragraph:

The light chain genes were switched to cDNA by the identical process used for the heavy chain. Oligonucleotide NX65 (GTTACGGGGCCCCTAACACTCTCCCCTGTTGAAG) (SEQ ID NO: 4), which anneals to the 3′ end of the kappa constant region, was used for reverse transcription and then NX65 and NXK1 (CAGCGTGCGGCCGCACCATGGACATCAGGGC_TCCTGCTCAG) (SEQ ID NO: 9) were used for PCR amplification of the entire kappa chain gene. The PCR product was inserted into p61.1 to form pNRX451. This plasmid is depicted in Figure 9.

Please replace the paragraph beginning at line 12 of page 56 with the following redlined paragraph:

The highest producing clone was selected (C2-451C4-100nM HP-2μM HP-161E12-50μM) and subjected to 2 rounds of limiting dilution cloning in 96-well plates in IMDM containing 10% dFBS and 50 μM Methotrexate before cell banking. The final clone was designated C2-451C4-100nM HP-2μM HP-161E12-50μM-12G4-3E7 (hybridoma producing the antibody was deposited with American Type Culture Collection (10801 University Blvd., Manassas, VA 20110) as ATCC Accession No. SD3273, converted to ATCC Accession No. CRL-12360.

Please replace the paragraph beginning at line 4 of page 63 with the following redlined paragraph:

The N-glycosylation site in the CH_2-domain of the human immunoglobulin heavy chain was site specific mutagenized by polymerase chain reaction (PCR). Oligonucleotides NX156 (5' AGCAGTAC **CAA** AGC ACG TAC CGG GTG 3') (SEQ ID NO: 10) and NX157 (5' TACGTGCT**TTG** GTA CTG CTC CTC 3') (SEQ ID NO: 11) were synthesized (DNAgency, Malvern, PA) to anneal to the coding (NX156) and noncoding (NX157) strands of the human heavy chain gene over the region containing the N-glycosylation site (Asn-Ser-Thr). Both oligonucleotides contained a two-base mismatch designed to mutate a codon from AAC (asparagine) to CAA (glutamine). In the first round of PCR, NX156 was paired with a downstream primer NX113 (5' GCTGACGGAT CCTCATTTAC CCGGAGACAG GGAG 3') (SEQ ID NO: 12) and NX157 was paired with an upstream primer NX110 (5' CCGTCTATTA CTGTTCTAGA GAGGTC 3') (SEQ ID NO: 13) in separate reactions using plasmid PNRX451 as a template and Ultma DNA polymerase according to the manufacturer's specifications (Perkin Elmer, Branchburg, NJ). The resulting PCR products were 476 base pairs for the NX110/NX157 primers and 634 base pairs for the NX156/NX113 primer pair; and comprised portions of the heavy chain extending upstream and downstream from the mutation, respectively. These PCR products were purified from agarose gels via Geneclean (Biolol, Vista, CA) and combined into a contiguous fragment in a second PCR using primers NX110 and NX113. The resulting PCR product was 1190 base pairs and contained the desired mutation. The product was digested with restriction enzymes SstII and BamHi to generate a 471 base pair fragment which was cloned into the expression vector pNRX451, replacing the N-glycosylation site containing wildtype gene fragment.